# EGLN1 gene

egl-9 family hypoxia inducible factor 1

## Normal Function

The *EGLN1* gene, often known as *PHD2*, provides instructions for making an enzyme called prolyl hydroxylase domain 2 (PHD2). The PHD2 enzyme interacts with a protein called hypoxia-inducible factor 2-alpha (HIF-2α). This protein is one part (subunit) of a larger HIF protein complex that plays a critical role in the body's ability to adapt to changing oxygen levels. HIF controls several important genes involved in cell division, the formation of new blood vessels, and the production of red blood cells. It is the major regulator of a hormone called erythropoietin, which controls red blood cell production.

The PHD2 enzyme's primary job is to target HIF-2α to be broken down (degraded) so it does not build up when it is not needed. When enough oxygen is available, the PHD2 enzyme is highly active to stimulate the breakdown of HIF-2α. However, when oxygen levels are lower than normal (hypoxia), the PHD2 enzyme becomes less active. As a result, HIF-2α is degraded more slowly, leaving more HIF available to stimulate the formation of new blood vessels and red blood cells. These activities help maximize the amount of oxygen that can be delivered to the body's organs and tissues.

Studies suggest that the *EGLN1* gene is involved in the body's adaptation to high altitude. At higher altitudes, such as in mountainous regions, air pressure is lower and less oxygen enters the body through the lungs. Over time, the body compensates for the lower oxygen levels by changing breathing patterns and producing more red blood cells and blood vessels.

Researchers suspect that the *EGLN1* gene may also act as a tumor suppressor gene because of its role in regulating cell division and other processes through its interaction with HIF. Tumor suppressors prevent cells from growing and dividing too fast or in an uncontrolled way, which could lead to the development of a tumor.

## Health Conditions Related to Genetic Changes

familial erythrocytosis

At least 10 mutations in the *EGLN1* gene have been found to cause familial erythrocytosis, an inherited condition characterized by an increased number of red blood cells and an elevated risk of abnormal blood clots. When familial erythrocytosis results from *EGLN1* gene mutations, it is often designated ECYT3.

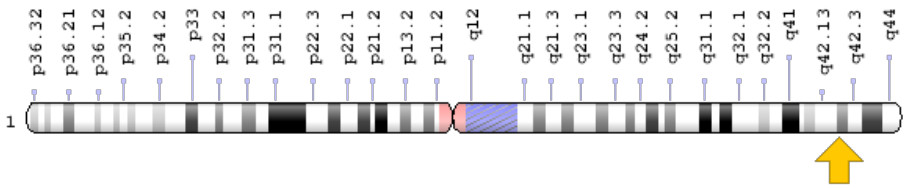
Some *EGLN1* gene mutations change single protein building blocks (amino acids) in the PHD2 enzyme, while others lead to the production of an abnormally short version of the enzyme. Any of these genetic changes disrupt the enzyme's ability to interact with HIF-2α and target it for destruction. Consequently, HIF accumulates in cells even when adequate oxygen is available. The presence of extra HIF leads to the production of red blood cells when no more are needed, resulting in an excess of these cells in the bloodstream.

At least one of the known *EGLN1* gene mutations has been associated with both familial erythrocytosis and a tumor called a paraganglioma in the same individual. Paragangliomas are noncancerous (benign) tumors of the nervous system. The mutation, written as His374Arg or H374R, replaces the amino acid histidine with the amino acid arginine at position 374 in the PHD2 enzyme. This genetic change alters the interaction between the PHD2 enzyme and HIF-2α, which leads to the production of excess red blood cells. However, it is unclear how the mutation may be associated with the development of paragangliomas.

## Chromosomal Location

Cytogenetic Location: 1q42.2, which is the long (q) arm of chromosome 1 at position 42.2

Molecular Location: base pairs 231,363,751 to 231,425,044 on chromosome 1 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)




Credit: Genome Decoration Page/NCBI

## Other Names for This Gene

- ECYT3
- egl-9 family hypoxia-inducible factor 1
- egl nine homolog 1
- egl nine homolog 1 (C. elegans)
- egl nine-like protein 1
- EGLN1_HUMAN

- HIF-PH2
- HIF-prolyl hydroxylase 2
- HIF prolyl hydroxylase 2
- HIFPH2
- HPH-2
- HPH2
- hypoxia-inducible factor prolyl hydroxylase 2
- PHD2
- prolyl hydroxylase domain-containing protein 2
- zinc finger MYND domain-containing protein 6
- ZMYND6

## Additional Information & Resources

Educational Resources

- National Cancer Institute: Pheochromocytoma and Paraganglioma
  https://www.cancer.gov/types/pheochromocytoma
- Palomar College: Adapting to High Altitude
  http://anthro.palomar.edu/adapt/adapt_3.htm
- The Cell: A Molecular Approach (second edition, 2000): Tumor Suppressor Genes
  https://www.ncbi.nlm.nih.gov/books/NBK9894/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28EGLN1%5BTIAB%5D%29+OR+%28PHD2%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- EGL9, C. ELEGANS, HOMOLOG OF, 1
  http://omim.org/entry/606425

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/EGLN1ID44140ch1q42.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=EGLN1%5Bgene%5D
- HGNC Gene Family: Zinc fingers MYND-type
  http://www.genenames.org/cgi-bin/genefamilies/set/87
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=1232
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/54583
- UniProt
  http://www.uniprot.org/uniprot/Q9GZT9

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